Armed Forces College of Medicine

AFCM

Gastrointestinal Pharmacology

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Lecture 5: Anti-diarrheai drugs

- ILOs:
  - Enumerate lines of therapy in treatment of diarrhea
  - Explain the maintenance of fluid and electrolyte balance
  - List the non specific anti-diarrheal agents
  - Explain the mechanism of action of non-specific anti-diarrheal agents
  - Enumerate the specific anti-diarrheal agents
  - List of the drugs used in treatment of ulcerative colitis

Treatment of Diarrhea:

- Maintenance of fluid and electrolyte balance in the first priority
- Specific Treatment of the cause:

  e.g.

  - Ciprofloxacin for shigella bacterial infection causing bacillary dysentery
  - Metronidazole for ameba causing amebic dysentery_
  - Doxycycline for vibrio cholera
- Non-Specific (Symptomatic) Treatment :Includes:
  - Correction of dehydration
  - GIT Protectives
  - Antimotility drugs

I- Correction of Dehydration: The main stay of therapy in cases of dehydration

A) In Mild & Moderate cases use **Oral Rehydration Therapy** (ORT):

1. ORT does ***NOT*** cure diarrhea, BUT ***ONLY*** corrects dehydration, acid/base & electrolyte imbalance.
2. Powder containing Glucose (4 g) + Na Cl (0.7 g) + K Cl (0.3 g) + Na citrate (0.51 g) to be dissolved in 200 ml water.

- The presence of glucose facilitates the absorption of Na^+, with subsequent absorption of Cl^- & H_2O.

B) In Severe cases use **Parenteral Rehydration** Therapy.

II- **GIT Protectives:** Adsorb toxic substances & provide a coating for the intestine

1. **Adsorbents**: Attraction or holding other materials on its surface

   Kaolin, Bismuth, Chalk & Charcoal.

2. **Absorbents** : Pectin, which is present in rice, carrots, apple.
3. **Astringents** : Causing contraction after topical application

   Tr. Catechu Release tannic acid in intestine & precipitate surface proteins.

III- Anti-Motility Agents:

1. **Parasympatholytics:** Atropine & Propantheline. For pain relief of intestinal colic

   Mechanism:

   - Antidiarrheal action: ↓ colonic peristalsis by blocking the response of intestinal smooth muscle to parasympathetic stimulation
   - Antispasmodic action: relieve cramps associated with diarrhea

2. **Opiates**: Diphenoxylate & Loperamide. For symptomatic control of diarrhea

   - Loperamide: Activates u opioid receptors in enteric nervous system with minimal CNS effects.
   - Diphenoxylate: similar to Loperamide but croses blood brain barrier in large doses .

   Mechanism:

   - They act on μ and (delta) receptors in the enteric nervous system leading to ↑ segmenting contractions of the small intestine.

3. **Racecadotril:** is an enkephalinase inhibitor it reduces hypersecretion of water & electrolytes into the intestinal lumen.

IV. Cholestyramine

Mechanism:

- It binds bile acids in the intestine preventing their absorption and decreasing their irritation

Therapeutic uses:

- Diarrhea due to bile salt malabsorption

□ **Treatment of Ulcerative Colitis:**

- Is characterized by intestinal mucosal inflammation

1. **Correct** anemia, dehydration, electrolyte & acid/base imbalance.
2. **Corticosteroids**: Orally, IV or Retention enema.
3. **Sulfasalazine**: Orally. A combination of Sulfapyridine & 5-Aminosalicylic acid which:
    A. NOT absorbed from small intestine.
    B. Split in colon by bacteria into :
    - Sulfapyridine Absorbed Most of side effects.
    - 5-Aminosalicylic acid Blocks LTB_4-Receptors Local anti-inflammatory effect.

4. **Mesalazine**: 5-Aminosalicylic acid. Taken orally. Safer than Sulfasalazine.

   Mechanism of action: may be inhibition of eicosanoid inflammatory mediators

5. **Olsalazine**: Two 5-Aminosalicylic acid linked together. Taken orally
6. **Natalizumab antibody:**
7. **Anti TNF drugs:** e.g. Infliximiab: neutralizes a protein produced by the immune system.
8. **Immuno modulators**: Azathioprine – Cyclosporin - Tacrolimus

□ Treatment of Colic = Antispasmodics:

1. **Parasympatholytics** e.g. Atropine and its antispasmodic substitutes: e.g. Propantheline
2. **Direct Spasmolytics**:
   - Volatile oils (peppermint), Kheline, papaverine
   - **Mebeverine** □ *Direct spasmolytic* □ Useful in colon spasm.

□ **Treatment of Biliary Colic:**

1. **Atropine & its substitutes** e.g. Hyoscine butyl bromide
2. **If severe pain**:

- Narcotic analgesics ▯ Morphine + Atropine (Never morphine alone) or Meperidine alone. Or Potent Antipyretic analgesics: NSAIDs as diclofenac IM

□ **Sialagogue** ▯ Drugs ▯ salivary secretions e.g. Pilocarpine ▯ Treat xerostomia.

□ **Anti-Sialagogues** ▯ Drugs ▯ salivation e.g. Atropine ▯ Useful in Pre-anesthetic medication & in treatment of Parkinsonism.

□ **Cholagogue** = Evacuate Gall bladder ▯ ▯ gall bladder contraction to evacuate gall bladder

1- **$MgSO_4$** (2-4 g before breakfast):
  a- Release Cholecystokinin ▯ Contract wall of gall bladder.
  b- Relax sphincter of Oddi.

2- **Fats & oils** → Release Cholecystokinin.

□ **Choleretics** = ▯ Synthesis of bile by heptocytes

1- Natural bile acids ▯ Cholic acid & desoxycholic acid.

2- Synthetic derivatives ▯ Na Glycocholate & Na Taurocholate.

- **Hydrochloretic** = ▯ Water in bile e.g. Salicylates & Dehydrocholic acid.

NB) Cholagogue & Choleretics:

1- **Useful in**:
  a- Flatulence b- Constipation c- Indigestion
  d- Help absorption of fat & fat soluble vitamins.

2- **Contraindications**: a- Obstructive jaundice b- Acute hepatitis

Lecture Quiz

Question 1 : The most likely reason why the majority of antacids contain Mg hydroxide & Al. hydroxide gel.

a) My hydroxide tends to cause a laxative effect that counteracts the tendency of an Al. salt to cause constipation.

Question 2: Pantoprazole may increase the risk of respiratory & enteric infections

a) Due to the loss of the anti bacterial properties of an acidic encrionment

Lecture Quiz

Question 3 : Liquid paraffin (a lubricant purgative) may cause hypoprothrombinemia

a) As it decreases absorption of fat soluble vitamins

Question 4: The use of Cimetidine is much less than ranitidine

b) Due to side effects present with Cimetidine only (gynecomastia, galactorrhea) of hepatic mic. enzymes & mental confusion in old age .

Lecture Quiz

Question 5 : Misoprostol prevents gastric ulcer induced by NSAID, but is never used during pregnancy

a) As it’s oxytocic, may cause abortion

Question 6: A pregnant lady (first trimester) comes to you with peptic ulcer disease. Which drug will you prescribe for her?

b) Antacids or sucralfate

Explanation

- H_2 antagonists cross placenta and are also secreted in breast milk
- Safety of Proton pump inhibitors not established in

Lecture Quiz

Question 7 : A patient comes to your clinic at midnight complaining of heart burn. You want to relieve his pain immediately. What drug will you choose?

a) Antacids

Explanation:

- Antacids neutralise the already secreted acid in the stomach
- All other drugs act by stopping acid secretion and so may not relieve symptoms at least for 45 min.

References and suggested books

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